REMARKS

Following entry of the above amendment, claims 40-59 will be pending, claims 1-19 having been canceled and claims 20-39 presented in the June 30, 2008, amendment but not entered. New claims 40-59 are modeled on claims 20-39, the support for which was described in detail in the June 30, 2008, amendment and so is not repeated here. Claims 40-59 are identical to non-entered claims 20-39 except that the reference to "the antibody" in part (i) of each of claims 40, 41, and 59 now says "the antibody of (a)." This does not change the scope at all with respect to corresponding claims 20, 21, and 39, and is added merely to clarify the claim. No new matter has been added. Applicants ask that the above amendment, which is intended to address an issue raised by the Examiner and his supervisor in a telephone conference with the undersigned on November 5, 2008, be entered so that prosecution can resume.

The Notice of Non-Responsive Amendment mailed October 20, 2008, asserts that claims 20-39 were drawn to a non-elected invention because they did not include the same "intended use" as the originally elected claims 1-8 and 13. Further reasons given are that claims 20-39 allegedly "do not share the same technical feature as the elected invention" and that the claims are allegedly "broader" (apparently because they do not include the same preamble) so their examination would be "burdensome." In the telephone conference of November 5, 2008, the undersigned pointed out that the limitations of the original independent claims 1 and 2 were present, albeit expressed differently, in independent claims 20, 21, and 39, so by definition claims 20, 21, and 39 included the same technical feature as the original claims. The undersigned offered to add the preamble language "A method for enhancing the activity of an antibody" into independent claims 20, 21, and 39, even though that was superfluous because an enhancement of activity compared to the original antibody was explicitly required in part (i) of each of these claims. A proposed amendment for discussion purposes was faxed to the Examiner on November 5, 2008; that proposed amendment added the preamble language and also modified "antibody" in some claims to read "original antibody," because the Examiner's supervisor had expressed some confusion about antecedence of the "antibody" in claim 20. In a subsequent telephone conference with the undersigned on November 10, 2008, the Examiner said that, upon

further study of the case in view of the standards for unity of invention, he and his supervisor were reformulating the issue. According to the Examiner, the problem now is that, in his view, the "invention" embodied in the original claims was better activity *vis a vis* the full antibody, while the "invention" embodied in the new claims is better activity *vis a vis* a two-chain diabody. The Examiner has concluded that claims 20-39 therefore lack unity of invention with respect to the original claims. The Examiner invited applicants to respond to this new argument in writing.

Original claim 1 read as follows:

> 1. A method for enhancing the activity of an antibody, which comprises making the antibody into a single-chain polypeptide comprising two or more light chain variable regions and two or more heavy chain variable regions linked via linkers.

Applicants point out that new independent claims 40 and 41 are drawn to methods that result in a single-chain polypeptide that contains two or more copies of the light and heavy chain variable regions of the starting (or "full", in the Examiner's terminology) antibody, linked via linkers. (Claim 59 is similar, except that it requires two or more copies of a "humanized version" of the light and heavy chain variable regions of the starting antibody.) Furthermore, claims 40, 41, and 59 all explicitly require that the resulting molecule (scFv multimer of claim 40 and single-chain polypeptide of claims 41 and 59) exhibit an activity at a level that is greater than the level exhibited by the starting antibody (i.e., the activity is "enhanced" compared to the activity of the starting antibody). Clearly, these claims contain whatever one might interpret to be the technical feature of the original claims. This simple, incontrovertible fact is not altered merely because applicants have chosen to further narrow the claims by adding another limitation specifying greater activity *vis a vis* a two-chain diabody.

Based on what the undersigned gleaned from the November 10, 2008, telephone conversation with the Examiner, it seems that the Examiner no longer challenges the above conclusions. Instead, the undersigned understands the Examiner to be taking the novel position that applicants are not entitled to add a new limitation to claims to overcome a rejection over prior art, as doing so would mean that the claims would acquire a new "technical feature" that is different from the "technical feature" of the claims before the new limitation was added, and so would lack unity of invention with the claims as they stood prior to adding that limitation.

Applicants submit that this would mean that claims in general could never be narrowed by adding new limitations to overcome a prior art rejection, a plainly nonsensical result. It is possible that applicants' representative has misunderstood the Examiner's position; if so, clarification in writing is requested.

Because it appears that the Examiner has agreed that adding the claim 1 preamble to each of claims 40, 41, and 59 is unnecessary and would be superfluous because the activity limitation is explicit in part (i) of each claim, the present amendment does not add it. If applicants have misunderstood the Examiner on this point, the preamble language can be added.

New independent claim 55 was not included in the above discussion because, unlike the other new independent claims, claim 55 does not contain all the limitations of original claim 1. Claim 55 does not require that two or more light chains and two or more heavy chains derived from a single starting antibody be included in the sc(Fv)2; rather, one pair of light and heavy chains is derived from a first antibody and a second pair is derived from a second antibody. Also, there is no limitation comparing the level of activity of the resulting sc(Fv)2 to the level of activity of either starting antibody. Accordingly, applicants acknowledge that the arguments put forth above regarding unity of invention do not apply to claim 55. Nevertheless, applicants submit that examination of new claim 55 and its dependent claims 56-58 along with the rest of the claims would not be unduly burdensome on the Examiner, so that inclusion of claims 55-58 in the present group would be reasonable. It is also noted that the prior Examiner assigned to this application, Examiner Gussow, reviewed with her supervisor a set of claims essentially identical to claims 20-39 (and thus to claims 40-59) and informed applicants by telephone on June 25, 2008, that the claims were indeed within the same restriction group as original claims 1-8 and 13, so could be presented in this application. That interview with Examiner Gussow and her supervisor is described on pages 7-8 of the Reply filed by applicants on June 30, 2008.

Applicants respectfully request that new claims 40-59 as presented herein be entered, examined, and allowed.

It is believed that no fees are due. If this is incorrect, please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: November 17, 2008_____

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